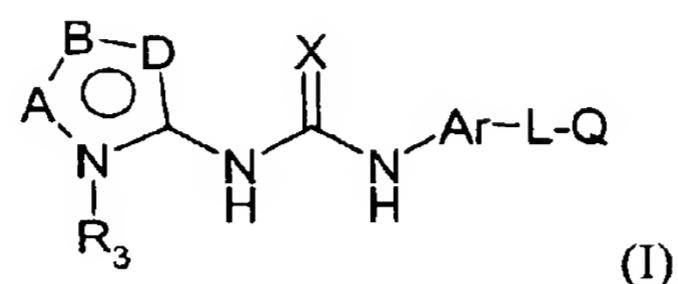


### What is claimed is:

1. A process of making a compound of the formula (I):

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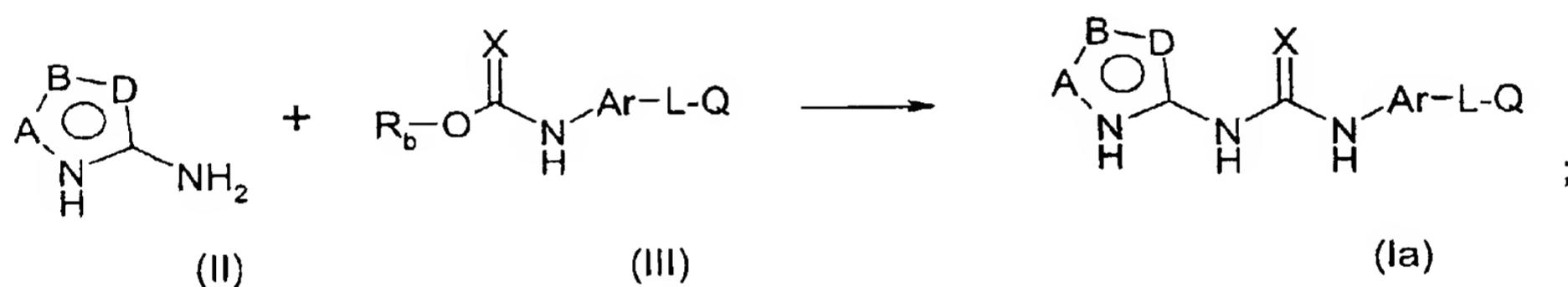


said process comprising:

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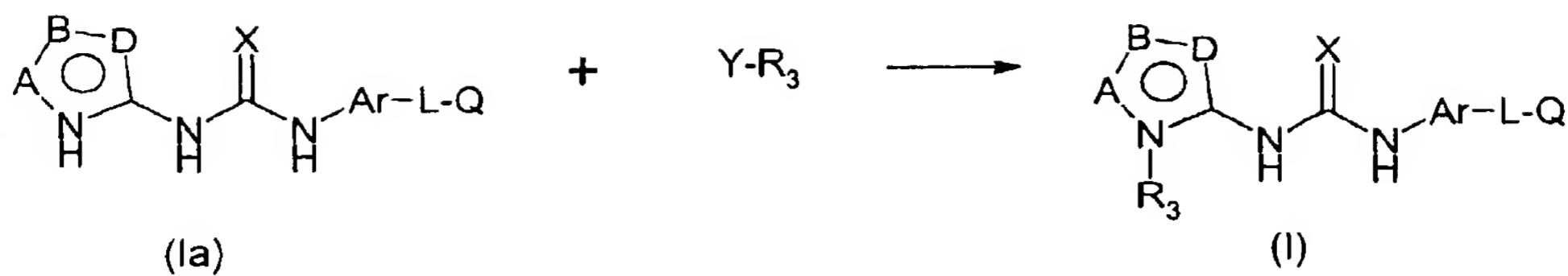
1) reacting an intermediate compound of the formula (III) with a heteroarylamine compound of the formula (II), said reaction occurring in the presence of a suitable base, in a polar non-protic organic solvent and at a suitable temperature of about 40-100°C for a reaction time of about 1 to 20 hours, to form an intermediate compound of the formula (Ia):

15



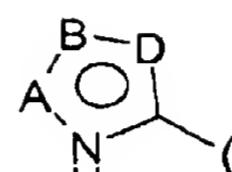
20 wherein  $R_b$  represents phenyl or a  $C_{2-3}$  halocarbon;

2) coupling the product of step 1), formula (Ia), with electrophile Y-R<sub>3</sub>, wherein the moiety Y is a group selected from BR<sub>2</sub>, BR<sub>3</sub>M, SiR<sub>3</sub> and SnR<sub>3</sub> wherein R is C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxy, hydroxy or halogen and wherein M is Na, Li or K, said coupling reaction occurring in a suitable base, and in the presence of a suitable catalyst; and said coupling reaction occurring at a suitable temperature of about 20-30°C. in a suitable solvent, to form a compound of the formula (I):

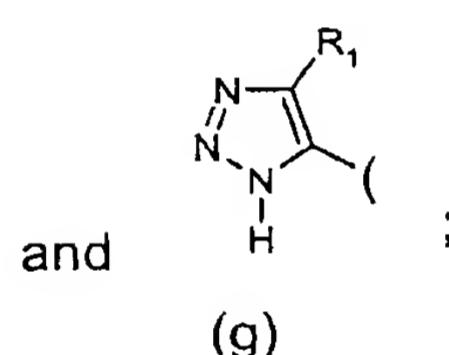
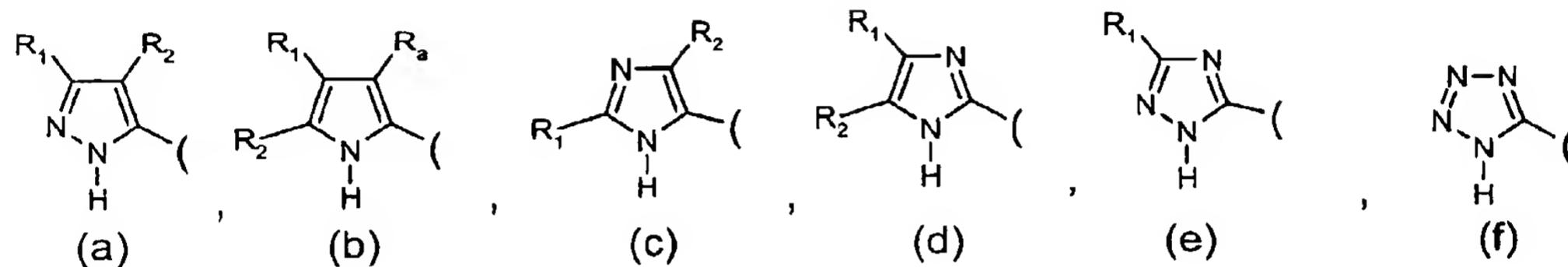


wherein:

5



the heteroaryl ring in formulas (I), (Ia) and (II):



10

wherein for the above heteroaryl rings (a), (b) and (d), R<sub>1</sub> and R<sub>2</sub> or R<sub>a</sub> can join to form a benzo ring fused to the heterocyclic ring to form a bicyclic heteroaryl;

15

Ar is:

phenyl, naphthyl, quinoline, isoquinoline, tetrahydronaphthyl, benzofuran, indanyl, indenyl or indole each being optionally substituted with one to three R<sub>2</sub> groups;

L, a linking group, is:

20

a bond or a C<sub>1-10</sub> saturated or unsaturated branched or unbranched carbon chain, wherein one or more C atoms are optionally replaced by O, N, or S(O)<sub>m</sub>; and wherein L is optionally partially or fully halogenated and optionally independently substituted

with one to two oxo groups, nitrile, phenyl or one or more C<sub>1-4</sub> alkyl optionally substituted by one or more halogen atoms;

or L is a cyclic group which is:

a) a C<sub>5-8</sub> cycloalkyl or cycloalkenyl optionally substituted with 1-2 oxo groups, 1-3

5 C<sub>1-4</sub> branched or unbranched alkyl or C<sub>1-4</sub> alkoxy;

b) phenyl, furan, thiophene, pyridine, pyrimidine, pyridinone, dihydropyridinone, maleimide, dihydromaleimide or pyrazine each being optionally independently substituted with 1-3 C<sub>1-4</sub> branched or unbranched alkyl, C<sub>1-4</sub> alkoxy, cyano, di-(C<sub>1-3</sub> alkyl)amino, C<sub>1-6</sub> alkyl-S(O)<sub>m</sub>, or halogen;

10 wherein said cyclic group is optionally attached to a C<sub>1-4</sub> saturated or unsaturated branched or unbranched carbon chain wherein said carbon chain is in turn covalently attached to Q, said carbon chain is optionally partially or fully halogenated and wherein one or more methylene groups are optionally replaced by O, N, S(O)<sub>m</sub>, wherein said methylene groups are further optionally independently substituted with 15 1-2 oxo groups and one or more C<sub>1-4</sub> branched or unbranched alkyl optionally substituted by one or more halogen atoms;

Q is selected from the group consisting of:

phenyl, naphthyl, pyridine, pyrimidine, pyridazine, furan, thiophene, pyran,

20 naphthyridine and oxazo[4,5-*b*]pyridine which are optionally substituted with one to three groups selected from the group consisting of halogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, di-(C<sub>1-3</sub> alkyl)amino and C<sub>1-6</sub> alkyl-S(O)<sub>m</sub>;

tetrahydropyran, tetrahydrofuran, 1,3-dioxolanone, 1,3-dioxanone, 1,4-dioxane, *N*-

25 morpholine, *N*-thiomorpholine, *N*-thiomorpholine sulfoxide, *N*-thiomorpholine sulfone, cyclohexanone, cyclohexanol, pentamethylene sulfide, pentamethylene sulfoxide, pentamethylene sulfone, tetramethylene sulfide, tetramethylene sulfoxide and tetramethylene sulfone which are optionally substituted with one to three groups selected from the group consisting of C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, di-(C<sub>1-3</sub> alkyl)amino-C<sub>1-3</sub> alkyl, and C<sub>1-3</sub> alkoxy-C<sub>1-3</sub> alkyl;

30 C<sub>1-6</sub> alkoxy, tertiary amine wherein the amino nitrogen is covalently bonded to groups selected from the group consisting of C<sub>1-3</sub> alkyl and C<sub>1-5</sub> alkoxyalkyl and phenyl wherein the phenyl ring is optionally substituted with one to two groups selected from

the group consisting of halogen, C<sub>1-6</sub> alkoxy, di-(C<sub>1-3</sub> alkyl)amino, C<sub>1-6</sub> alkyl-S(O)<sub>m</sub> and phenyl-S(O)<sub>m</sub>, wherein the phenyl ring is optionally substituted with one to two groups consisting of halogen, C<sub>1-6</sub> alkoxy, or di-(C<sub>1-3</sub> alkyl)amino;

5 R<sub>1</sub> is selected from the group consisting of:

C<sub>3-10</sub> branched or unbranched alkyl, which may optionally be partially or fully halogenated, and optionally substituted with one to three phenyl, naphthyl or heterocyclic groups selected from the group consisting of pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thienyl, furyl, isoxazolyl and isothiazolyl; each such phenyl, naphthyl or heterocycle selected from the group hereinabove described, being substituted with 0 to 5 groups selected from the group consisting of halogen, C<sub>1-6</sub> branched or unbranched alkyl which is optionally partially or fully halogenated, C<sub>3-8</sub> cycloalkyl, C<sub>5-8</sub> cycloalkenyl, cyano, C<sub>1-3</sub> alkyloxy which is optionally partially or 10 fully halogenated and di(C<sub>1-3</sub>)alkylaminocarbonyl;

C<sub>3-7</sub> cycloalkyl selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentanyl, cyclohexanyl, cycloheptanyl, bicyclopentanyl, bicyclohexanyl and bicycloheptanyl, which are optionally partially or fully halogenated and optionally substituted with one to three C<sub>1-3</sub> alkyl groups, or an analog of such cycloalkyl group 20 wherein one to three ring methylene groups are replaced by groups independently selected from O, S, >C=O and >C=S;

C<sub>3-10</sub> branched alkenyl optionally partially or fully halogenated, and optionally 25 substituted with one to three C<sub>1-5</sub> branched or unbranched alkyl, phenyl, naphthyl or heterocyclic groups, with each such heterocyclic group being independently selected from the group consisting of pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thienyl, furyl, isoxazolyl and isothiazolyl, and each such phenyl, naphthyl or heterocyclic group being substituted with 0 to 5 groups selected from halogen, C<sub>1-6</sub> branched or unbranched alkyl which is optionally partially or fully halogenated, cyclopropyl, cyclobutyl, cyclopentanyl, cyclohexanyl, cycloheptanyl, bicyclopentanyl, 30 bicyclohexanyl, bicycloheptanyl, cyano, C<sub>1-3</sub> alkyloxy which is optionally partially or fully halogenated and di(C<sub>1-3</sub>)alkylaminocarbonyl;

*C<sub>5-7</sub> cycloalkenyl selected from the group consisting of cyclopentenyl, cyclohexenyl, cyclohexadienyl, cycloheptenyl, cycloheptadienyl, bicyclohexenyl and bicycloheptenyl, wherein such cycloalkenyl group is optionally substituted with one to three C<sub>1-3</sub> alkyl groups;*

5    *cyano; and,*  
*methoxycarbonyl, ethoxycarbonyl and propoxycarbonyl;*

*R<sub>2</sub> is selected from the group consisting of:*

10    *a C<sub>1-6</sub> branched or unbranched alkyl optionally partially or fully halogenated, acetyl, aroyl, C<sub>1-4</sub> branched or unbranched alkoxy optionally partially or fully halogenated, halogen and methoxycarbonyl;*

*R<sub>3</sub> is selected from the group consisting of:*

15    *a phenyl, naphthyl or heteroaryl group selected from the group consisting of pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, thienyl, furyl, tetrahydrofuryl, isoxazolyl, isothiazolyl, quinolinyl, isoquinolinyl, indolyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, benzothiofuranyl, cinnolinyl, pterindinyl, phthalazinyl, naphthypyridinyl, quinoxaliny, quinazolinyl, purinyl and indazolyl wherein such phenyl, naphthyl or heteroaryl group is optionally substituted with one to five groups*

20    *selected from the group consisting of a C<sub>1-6</sub> branched or unbranched alkyl, phenyl, naphthyl, heteroaryl group selected from the groups hereinabove described, C<sub>1-6</sub> branched or unbranched alkyl which is optionally partially or fully halogenated, cyclopropyl, cyclobutyl, cyclopentanyl, cyclohexanyl, cycloheptanyl, bicyclopentanyl, bicyclohexanyl, bicycloheptanyl, phenyl C<sub>1-5</sub> alkyl, naphthyl C<sub>1-5</sub>*

25    *alkyl, halo, cyano, C<sub>1-3</sub> alkyloxy which may optionally be partially or fully halogenated, phenoxy, naphthoxy, heteroxyloxy wherein the heterocyclic moiety is selected from the group hereinabove described, nitro, di-(C<sub>1-3</sub>)alkylamino, di-(C<sub>1-3</sub>)alkyl aminocarbonyl, C<sub>1-5</sub> alkyl-C(O)-C<sub>1-4</sub> alkyl, di-(C<sub>1-3</sub>)alkylamino-C<sub>1-5</sub> alkyl, di-(C<sub>1-3</sub>)alkylamino-S(O)<sub>2</sub>, R<sub>4</sub>-C<sub>1-5</sub> alkyl, R<sub>5</sub>-C<sub>1-5</sub> alkoxy, R<sub>6</sub>-C(O)-C<sub>1-5</sub> alkyl and R<sub>7</sub>-C<sub>1-5</sub>*

30    *alkyl-N(R<sub>8</sub>); and*

*a fused aryl selected from the group consisting of benzocyclobutanyl, indanyl, indenyl, dihydronaphthyl, tetrahydronaphthyl, benzocycloheptanyl and benzocycloheptenyl, or a fused heterocyclyl selected from cyclopentenopyridine,*

cyclohexanopyridine, cyclopentanopyrimidine, cyclohexanopyrimidine,  
cyclopentanopyrazine, cyclohexanopyrazine, cyclopentanopyridazine,  
cyclohexanopyridazine, cyclopentanoquinoline, cyclohexanoquinoline,  
cyclopentanoisoquinoline, cyclohexanoisoquinoline, cyclopentanoindole,  
5 cyclohexanoindole, cyclopantanobenzoxazole, cyclohexanobenzoxazole,  
cyclopentanothiophene and cyclohexanothiophene; wherein the fused aryl or fused  
heterocycl ring is substituted with 0 to 3 groups independently selected from  
phenyl, naphthyl, heterocycl selected from the group consisting of pyridinyl,  
pyrimidinyl, pyrazinyl, pyridazinyl, thienyl, furyl, isoxazolyl, and isothiazolyl, C<sub>1-6</sub>  
10 branched or unbranched alkyl which is optionally partially or fully halogenated, halo,  
cyano, C<sub>1-3</sub> alkyloxy which is optionally partially or fully halogenated, phenoxy,  
naphthoxy, heterocyclyoxy wherein the heterocycl moiety is selected from the  
group hereinabove described, nitro, di-(C<sub>1-3</sub>)alkylamino, di-(C<sub>1-3</sub>)alkyl aminocarbonyl,  
C<sub>1-4</sub> alkyl-OC(O), C<sub>1-5</sub> alkyl-C(O)-C<sub>1-4</sub> branched or unbranched alkyl, di-(C<sub>1-</sub>  
15 3)alkylamino-C<sub>1-5</sub> alkyl, R<sub>9</sub>-C<sub>1-5</sub> alkyl, R<sub>10</sub>-C<sub>1-5</sub> alkoxy, R<sub>11</sub>-C(O)-C<sub>1-5</sub> alkyl and R<sub>12-</sub>  
C<sub>1-5</sub> alkyl-N(R<sub>13</sub>)-;

R<sub>1</sub> and R<sub>2</sub> taken together optionally form a fused phenyl or pyridinyl ring;

20 each R<sub>8</sub> or R<sub>13</sub> is independently C<sub>1-4</sub> branched or unbranched alkyl optionally partially  
or fully halogenated;

each R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>9</sub>, R<sub>10</sub>, R<sub>11</sub> and R<sub>12</sub> is independently selected from the  
group consisting of:

25 N-morpholine and piperazine;

R<sub>a</sub> equals the definitions of R<sub>1</sub>, wherein R<sub>a</sub> and R<sub>1</sub> can be simultaneously the same or  
different;

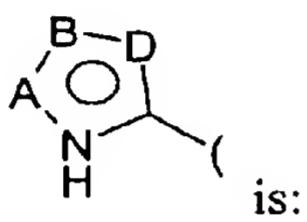
30 each m is independently 0, 1 or 2;

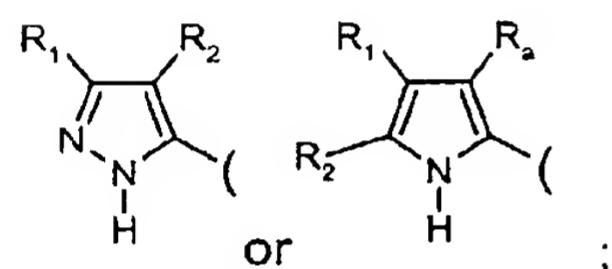
X is O or S.

2. The process according to claim 1 wherein wherein Ar is naphthyl, tetrahydronaphthyl, indanyl or indenyl.

5 3. The process according to claim 2 wherein Ar is naphthyl.

4. The process according to claim 3 wherein

10 the heteroaryl ring  is:



Ar is 1-naphthyl;

15 L is C<sub>1-6</sub> saturated or unsaturated branched or unbranched carbon chain wherein

one or more C atoms are optionally replaced by O, N or S(O)<sub>m</sub>; and wherein said linking group is optionally substituted with one to two oxo groups, C<sub>1-4</sub> alkyl optionally substituted by one or more halogen atoms;

20 or L is cyclopentenyl, cyclohexenyl, cycloheptenyl, each optionally substituted with an oxo group or 1-3 C<sub>1-4</sub> branched or unbranched alkyl or C<sub>1-4</sub>alkoxy; or L is phenyl, pyridine, furan or thiophene each being optionally independently substituted with 1-3 C<sub>1-4</sub> branched or unbranched alkyl, C<sub>1-4</sub>alkoxy, cyano, di-(C<sub>1-3</sub> alkyl)amino, C<sub>1-6</sub> alkyl-S(O)<sub>m</sub> or halogen;

25 wherein said cyclic group is optionally attached to a C<sub>1-4</sub> saturated or unsaturated branched or unbranched carbon chain wherein said carbon chain is in turn covalently attached to Q, said carbon chain is optionally partially or fully halogenated and wherein one or more methylene groups are optionally replaced by O, N or S(O)<sub>m</sub>, wherein said methylene groups are further optionally independently substituted with

1-2 oxo groups and one or more C<sub>1-4</sub> branched or unbranched alkyl optionally substituted by one or more halogen atoms;

R<sub>1</sub> is C<sub>3-4</sub>alkyl branched or unbranched, cyclopropyl or cyclohexanyl  
5 optionally partially or fully halogenated and optionally substituted with one to three C<sub>1-3</sub> alkyl groups;

R<sub>3</sub> is selected from the group consisting of phenyl, pyridinyl each being optionally substituted with one to five groups selected from the group consisting of a C<sub>1-6</sub> branched or unbranched alkyl, phenyl, 10 naphthyl, pyridinyl, C<sub>1-6</sub> branched or unbranched alkyl, cyclopropyl, cyclobutyl, cyclopentanyl, cyclohexanyl, cycloheptanyl, bicyclopentanyl, bicyclohexanyl, bicycloheptanyl, phenyl C<sub>1-5</sub> alkyl, naphthyl C<sub>1-5</sub> alkyl, halo, cyano, C<sub>1-3</sub> alkyloxy which may optionally be partially or fully halogenated, phenoxy, naphthoxy, pyridinyloxy, nitro, di-(C<sub>1-3</sub>)alkylamino, di-(C<sub>1-3</sub>)alkyl aminocarbonyl, C<sub>1-5</sub> alkyl-15 C(O)-C<sub>1-4</sub> alkyl, di-(C<sub>1-3</sub>)alkylamino-C<sub>1-5</sub> alkyl, di-(C<sub>1-3</sub>)alkylamino-S(O)<sub>2</sub>, R<sub>4</sub>-C<sub>1-5</sub> alkyl, R<sub>5</sub>-C<sub>1-5</sub> alkoxy, R<sub>6</sub>-C(O)-C<sub>1-5</sub> alkyl and R<sub>7</sub>-C<sub>1-5</sub> alkyl-N(R<sub>8</sub>)-.

5. The process according to claim 4 wherein

20

L is:

O-CH<sub>2</sub>-, O-CH<sub>2</sub>CH<sub>2</sub>, O-CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, O-CH<sub>2</sub>CH<sub>2</sub>(CH<sub>3</sub>), O-CH<sub>2</sub>(CH<sub>3</sub>)CH<sub>2</sub>, S(O)<sub>m</sub>CH<sub>2</sub>, S(O)<sub>m</sub>CH<sub>2</sub>CH<sub>2</sub>, S(O)<sub>m</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, O-CH<sub>2</sub>C(O),

25

HC≡C—CH<sub>2</sub> or HC≡C—CH<sub>2</sub>O;

and Q is N-morpholino.

6. The process according to claim 5 wherein L is O-CH<sub>2</sub>CH<sub>2</sub>.

30

7. The process according to claim 6 wherein:

in step 1):

the suitable base is selected from triethylamine, diisopropylethylamine, N-methylpyrrolidine, DBU, DMAP, N-methylmorpholine, pyridine and methyl pyridine;

5 the polar non-protic organic solvent selected from NMP, acetonitrile, DMF, DMAc and DMSO;

the temperature is about 80°C;

10 the reaction time is 4-10 hours;

R<sub>b</sub> is 2,2,2-trichloroethyl;

in step 2):

Y-R<sub>3</sub> is present in about a two-fold molar excess, wherein Y is B(OH)<sub>2</sub>;

15 the suitable base is triethylamine or pyridine and is present in about a two-fold molar excess;

the suitable catalyst is Cu(OAc)<sub>2</sub>, (Cu(OH).TMEDA)<sub>2</sub>Cl<sub>2</sub> or CuCO<sub>3</sub>.Cu(OH)<sub>2</sub> and present at about a 1.5 molar excess;

20 the suitable solvent is selected from methylene chloride, 1,4-dioxane, N-methylpyrrolidinone, THF and DMF.

8. The process according to claim 7 wherein:

in step 1):

25 suitable base is diisopropylethylamine;

polar non-protic organic solvent is DMSO;

in step 2):

the suitable base is pyridine;

30 the suitable catalyst is Cu(OAc)<sub>2</sub>;

suitable solvent is methylene chloride.